

## Multidisciplinary Diagnostic Approach for Left Ventricular Hypertrabeculation/Noncompaction

Josef Finsterer<sup>1</sup>, Claudia Stöllberger<sup>2</sup>, and Wolfgang Kopsa<sup>3</sup>

<sup>1</sup>Department of Neurology, <sup>2</sup>2nd Medical Department, <sup>3</sup>Radiological Department, Krankenanstalt Rudolfstiftung, Vienna, Austria.

The report on three patients with asymptomatic left ventricular hypertrabeculation/noncompaction (LVHT) by Koh et al.<sup>1</sup> is stimulating but also raised the following concerns.

In light of recent reports about patients in whom LVHT developed during their lifetimes,<sup>2,3</sup> we regard discussing LVHT as a "congenital form of cardiomyopathy"<sup>1</sup> as unjustified. Though LVHT appears to be congenital in the majority of cases, particularly in cases involving children and young adults, it is verifiably acquired in single cases.<sup>2,3</sup> Unfortunately, the pathomechanism of LVHT has neither been discovered for the acquired nor the congenital form. The most frequently presumed and discussed pathomechanisms for acquired LVHT are: (1) it is a compensatory mechanism of an impaired myocardium or (2) it results from destruction of the impaired myocardium by the intra-ventricular pressure. Congenital LVHT is most frequently attributed to an arrest of the physiologic intrauterine compaction process during embryonic heart development.

Since long-term follow-up data about the diagnosis of LVHT are lacking, it is speculative to state that LVHT is associated with increased morbidity and mortality in the patients described by Koh et al.

Since it is under debate if LVHT is an indication for oral anti-coagulation, we propose oral anti-coagulation only if decreased systolic function or atrial fibrillation is also present. This approach is

substantiated by findings from a series of 62 patients of which thrombo-embolic events were found in only 10% of the patients with LVHT but in 15% of age-, sex- and left ventricular function-matched controls.<sup>4</sup>

LVHT is frequently found in patients with neuromuscular disorders. LVHT has been reported in association with Duchenne or Becker muscular dystrophy, myotonic dystrophy type 1, dystrobrevinopathy, Pompe's disease, myoadenylate-deaminase deficiency, mitochondriopathy, cypher gene mutations, centronuclear myopathy, Friedreich ataxia, Barth syndrome, or various other rare genetic disorders.<sup>5-10</sup>

Since atrio-ventricular block is a common feature of neuromuscular disorders with cardiac involvement, particularly in myotonic dystrophy, it appears essential to investigate each patient neurologically with appropriate examinations to exclude neuromuscular disorders as the underlying cause of LVHT.

It is stated that LVHT is an "extremely rare disorder".<sup>1</sup> However, in our experience LVHT is more prevalent than previously thought particularly if asymptomatic relatives of patients with proven LVHT also undergo cardiac examinations. In an adult echocardiographic laboratory the prevalence of LVHT amounted to 0.25%/year.<sup>11</sup> The true prevalence of LVHT among the general population is, however, unknown since no screening investigations have been carried out thus far.

Establishing the diagnosis of LVHT is dependent on the echocardiographer's awareness and experience, the applied transducer frequencies, and the applied diagnostic criteria. So far, three different definitions of LVHT have been proposed.<sup>5,12,13</sup> Since there is no consensus about the

Received November 22, 2004

Accepted December 4, 2004

Reprint address: requests to Dr. Josef Finsterer, Postfach 20  
1180 Wien, Austria, Europe. Tel: 43-1-71165-92085, Fax: 43-1-  
4781711, E-mail: duarte@aonmail.at

accuracy and applicability of these definitions, it is desirable to know if LVHT in the described patients also fulfils diagnostic criteria other than the applied. Furthermore, we cannot understand how the ratio between a non-compacted and a compacted layer can be easily calculated at end-systole, particularly in small, well-contracting left ventricles.

Cardiac computed tomography represents a radiographic technique with a high radiation burden. An additionally supplied contrast medium is cost expensive. Cardiac MRI carries a much lower risk for side effects.

Extensive trabeculations found at autopsy in 68% of normal hearts refers to a number of up to three trabeculations. More than three trabeculations were found in only 4% of the normal hearts.<sup>14</sup> The following anatomical findings were the bases for Stöllberger's LVHT definition: more than > 3 coarse, prominent trabeculations apically to the papillary muscles on echocardiography, which have the same echogenicity as the myocardium, move synchronously with it, are not connected to the papillary muscles, and are surrounded by intertrabecular spaces, which are perfused from the ventricular cavity.<sup>5</sup>

Finally, the diagnosis of a lumbar disc prolapse is questionable in a patient with bilateral radicular pain. Was there any indication for vertebral stenosis, discitis, or polyradiculitis? Did the patient's symptoms completely resolve after surgery?

In conclusion, LVHT is a rare cardiac abnormality of which the underlying etiology and pathomechanism are poorly understood. LVHT requires special attention not only of the cardiologist but also of the neurologist. Furthermore, special consideration is also required of the pediatrician in childhood and juvenile cases.

## REFERENCES

1. Koh YY, Seo YU, Woo JJ, Chang KS, Hong SP. Familial isolated noncompaction of the ventricular myocardium in asymptomatic phase. *Yonsei Med J* 2004;45:931-5.
2. Finsterer J, Stöllberger C. Spontaneous left ventricular hypertrabeculation in Dystrophin duplication based Becker muscular dystrophy. *Herz* 2001;26:477-81.
3. Finsterer J, Stöllberger C, Schubert B. Acquired left ventricular hypertrabeculation/noncompaction in mitochondrialriopathy. *Cardiology* 2004;102:228-30.
4. Stöllberger C, Finsterer J. Left ventricular hypertrabeculation/noncompaction and stroke or embolism. *Cardiology* 2005;103:68-72.
5. Stöllberger C, Finsterer J. Left ventricular hypertrabeculation/noncompaction. *J Am Soc Echocardiogr* 2004;17:91-100.
6. Alper G, Narayanan V. Friedreich's ataxia. *Pediatr Neurol* 2003;28:335-41.
7. Finsterer J, Stöllberger C, Blazek G. Left ventricular noncompaction suggests myopathy. *Circulation* 2004;109:e201-e2.
8. Ichida F, Tsubata S, Bowles KR, Handeda N, Uese K, Miyawaki T, et al. Novel gene mutations in patients with left ventricular noncompaction or Barth Syndrome. *Circulation* 2001;103:1256-63.
9. Pipo JR, Feng JH, Yamamoto T, Ohsaki Y, Nanba E, Tsujino S, et al. New GAA mutations in Japanese patients with GSDII (Pompe disease). *Pediatr Neurol* 2003;29:284-7.
10. Vatta M, Mohapatra B, Jimenez S, Sanchez X, Faulkner G, Perles Z, et al. Mutations in Cypher/ZASP in patients with dilated cardiomyopathy and left ventricular non-compaction. *J Am Coll Cardiol* 2003;42:2014-27.
11. Stöllberger C, Finsterer J. Cardiologic and neurologic findings in left ventricular hypertrabeculation/noncompaction related to wall thickness, size and systolic function. *Eur J Heart Fail* 2005;7:95-7.
12. Chin TK, Perloff JK, Williams RG, Jue K, Mohrmann R. Isolated noncompaction of left ventricular myocardium. A study of eight cases. *Circulation* 1990;82:507-13.
13. Oechslin EN, Attenhofer Jost CH, Rojas JR, Kaufmann PA, Jenni R. Long term follow-up of 34 adults with isolated left ventricular noncompaction: A distinct cardiomyopathy with poor prognosis. *J Am Coll Cardiol* 2000;36:493-500.
14. Boyd MT, Seward JB, Tajik AJ, Edwards WD. Frequency and location of prominent left ventricular trabeculations at autopsy in 474 normal human hearts: Implications for evaluation of mural thrombi by two-dimensional echocardiography. *J Am Coll Cardiol* 1987;9:323-6.

## Author Reply

**Young Youp Koh**

*Department of Cardiology, Chosun University, College of Medicine, Gwangju, Korea.*

I read with interest Finsterer's letter to the editor about our work. In his letter, Finsterer

questions the incidence of isolated noncompaction of the ventricular myocardium (INVM), the pathomechanism of left ventricular hypertrabeculation (LVHT)/ INVM, the usefulness of multidetector CT (MD CT) compared with cardiac MRI as the diagnostic modality, the diagnostic criteria, and whether or not neuromuscular disorders exist in our cases. As we have stated, INVM is a rare congenital form of cardiomyopathy resulting from an intrauterine arrest in the normal process of trabecular compaction of the myocardium.<sup>1</sup> The incidence of INVM, referred to also as "persistent endomyocardial sinusoidal myocardium", "spongy myocardium", or "left ventricular hypertrabeculation" is sporadic; however in some patients it may be due to chromosomal abnormalities and familial incidence may occur.<sup>2-7</sup> LVHT is frequently found in patients with neuromuscular disorders.<sup>8</sup> In our experience, familial INVM regarded as a "congenital form of cardiomyopathy" was demonstrated in three adult members incidentally.<sup>7</sup> Although INVM is a rare disorder, to date, its prevalence as an isolated entity seems to be steadily increasing as physicians and echocardiographers become more aware of its possibility and as cardiac imaging modalities become more effective. The method of choice to identify INVM is echocardiography because it can reveal prominent trabeculations and deep intertrabecular recesses, which are lined with thick endocardium and communicate with the left ventricular cavity in the absence of other congenital or acquired heart disease.<sup>9</sup> Excessive trabeculations have been reported in 68% of normal hearts, and INVM must be differentiated from prominent normal myocardial trabeculation, hypertrophic or dilated cardiomyopathy (DCM), and left ventricular apical thrombus.<sup>10</sup> Two different definitions of INVM were proposed in the 1990s, yet neither have been fully accepted in clinical practice.<sup>1,9</sup> Chin et al.<sup>1</sup> introduced coefficient X/Y for objective assessment of the deepness of intertrabecular recesses and Oechslin et al.<sup>9</sup> introduced the end systolic ratio of noncompacted / compacted zones (N/C ratio). A N/C ratio >2 was accepted as typical for INVM, and in our case it was 2.62.<sup>7</sup> In a normal prominent myocardial trabeculation, the trabecules are single and no recesses are present, unlike the case with INVM. Thus, another diagnostic cri-

terium is needed, and we agree with Stöllberger's LVHT definition: more than 3 coarse and prominent trabeculations apically to the papillary muscles on echocardiography, which have the same echogenicity as the myocardium, move synchronously with it, are not connected to the papillary muscles, and are surrounded by intertrabecular spaces perfused from the ventricular cavity.<sup>8</sup> Nowadays, cardiac tomography such as multidetector CT and cardiac MRI seem to be useful complementary tools when a definite diagnosis cannot be made. MD CT may show the typical morphological features of noncompaction with higher spatial and temporal resolution and shorter image acquisition time compared with cardiac MRI.<sup>11,12</sup> There is no specific treatment option for noncompaction cardiomyopathy, but can include all options available for the treatment of heart failure. We agree with Finsterer regarding the need for oral anti-coagulation for INVM with left ventricular systolic dysfunction, atrial arrhythmia, and local thrombi within the deep intertrabecular recesses, due to the increased risk of systemic embolism. On the other hand, in our case an intervertebral herniated disc was diagnosed at the L5-S1 level with MRI, and the patient's symptoms were completely resolved surgically, with no limitation in ordinary activity. In conclusion, it was the focus of our report to emphasize familial occurrence of INVM, incidental diagnosis of INVM in asymptomatic phase with conventional echocardiography and cardiac MD CT, and the importance of screening first-degree relatives of the patient.

## REFERENCES

1. Chin TK, Perloff JK, Williams RG, Jue K, Mohrmann R. Isolated noncompaction of left ventricular myocardium. A study of eight cases. *Circulation* 1990;82:507-13.
2. Bleyl SB, Mumford BR, Thompson V, Carey JC, Pysher TJ, Chin TK. et al. Neonatal, lethal noncompaction of the left ventricular myocardium is allelic with Barth syndrome. *Am J Hum Genet* 1997;61:868-72.
3. Bleyl SB, Mumford BR, Brown-Harrison MC, Pagotto LT, Carey JC, Pysher TJ, et al. Xq28-linked noncompaction of the left ventricular myocardium: prenatal diagnosis and pathologic analysis of affected individuals. *Am J Med Genet* 1997;72:257-65.

4. Matsuda M, Tsukahara M, Kondo O, Mito H. Familial isolated noncompaction of ventricular myocardium. *J Hum Genet* 1999;44:126-8.
5. Oechslin E, Attenhofer C, Rohas J, Kauffman P, Jenni R. Long-term follow-up of 34 adults with isolated left ventricular noncompaction: A distinct cardiomyopathy with poor prognosis. *J Am Coll Cardiol* 2000;36:493-500.
6. Ichida F, Tsubata S, Boweles K, Heneda N, Boweles N, Towbin J. Novel gene mutations in patients with left ventricular non-compaction or Barth syndrome. *Circulation* 2001;103:1256.
7. Koh YY, Seo YU, Woo JJ, Chang KS, Hong SP. Familial isolated noncompaction of the ventricular myocardium in asymptomatic phase. *Yonsei Med J* 2004;45:931-5.
8. Stöllberger C, Finsterer J. Left ventricular hypertrabeculation/noncompaction. *J Am Soc Echocardiogr* 2004;17: 91-100.
9. Oechslin E, Attenhofer C, Rohas J, Kauffman P, Jenni R. Long-term follow-up of 34 adults with isolated left ventricular noncompaction: A distinct cardiomyopathy with poor prognosis. *J Am Coll Cardiol* 2000;36:493-500.
10. Boyd BT, Seward JB, Tajik AJ, Edwards WD. Frequency and location of prominent left ventricular trabeculations in autopsyin 474 normal human hearts: Implication for evaluation of mural thrombi by two-dimensional echocardiography. *J Am Coll Cardiol* 1987;9:323-26.
11. Ohnesorge BM, Becker CR, Flohr TG, Reiser MF. Multi-slice CT in cardiac imaging. technical principles, clinical application and future developments. Munich: Springer, 2002.
12. Soler R, Rodriguez E, Monserrat L, Alvarez N. MRI of subendocardial perfusion deficits in isolated left ventricular noncompaction. *J Comput Assist Tomogr* 2002;26: 373-75.